

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
(Case No. 96,877-V1)

In the Application of:)	
)	
Robert T. Lum et al.)	
)	Art Unit: 1624
Serial No.: Unknown)	
)	Examiner: M. Berch
Filed: August 14, 2001)	
)	
Title: Purine Inhibitors of Cyclin Dependent)	
Kinase 2 and I κ b- α)	
Laminate Materials)	

PRELIMINARY AMENDMENT

Dear Sir:

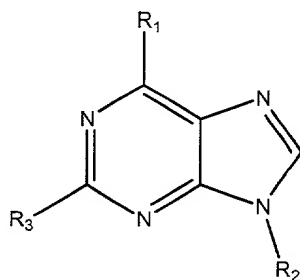
This Preliminary Amendment accompanies the Continuation application filed on August 13, 2001. Please amend the application as follows before calculating the application filing fee:

IN THE CLAIMS:

Cancel claims 1-47 from the application without prejudice.

Add the following new claims 48-76 to the application:

48. (New) A compound having the formula:



wherein

R₁ is -X-R₁';

in which R₁' is lower alkyl, substituted lower alkyl, cycloalkyl, substituted cycloalkyl, cycloheteroalkyl, substituted cycloheteroalkyl, aryl, substituted aryl, aralkyl, substituted

aralkyl, hetaryl, substituted hetaryl, heteroalkyl, and substituted heteroalkyl;

and X is -NH-, -O-, -S-, or -SO₂;

R₂ is lower alkyl optionally substituted with one, two or three groups selected from hydroxy, alkoxy, halogen, mercapto, alkylthiol, amino, amido, carboxy, cyano, aryloxy, alkenyl, alkynyl, or acyl; or

aryl, heteroaryl, arylalkyl or heteroarylalkyl where the ring portion of each is optionally substituted with one, two or three groups selected from lower alkyl, alkoxy, halogen, mercapto, alkylthiol, ethynyl, amino, amido, carboxy, hydroxy, aryl, aryloxy, heteroaryl, nitro, or cyano; or cycloalkyl optionally substituted with one, two or three groups selected from lower alkyl, alkoxy, halogen, thiol, ethynyl, alkylthiol, aryl, aryloxy, heteroaryl, nitro, or cyano; or heterocyclyl;

and

R₃ is halogen, hydroxy, mercapto, alkoxy, alkylthiol, lower alkyl, or -NR₄R₅;

in which R₄ and R₅ independently are hydrogen or lower alkyl optionally substituted with one, two or three groups selected from hydroxy, alkoxy, halogen, amino, mercapto, alkylthiol, amido, carboxyl, cyano, aryloxy, or acyl, or;

aryl, arylalkyl, heteroaryl, heteroarylalkyl, or cycloalkyl where the ring portion of each is optionally substituted with one, two or three groups selected from lower alkyl, alkoxy, halogen, mercapto, alkylthiol, ethynyl, amino, amido, carboxyl, hydroxy, aryl, aryloxy, heteroaryl, nitro, or cyano;

with the proviso that when R₁ is benzyl, X is -NH-, and R₂ is lower alkyl of C₁₋₄, R₃ is not lower alkyl of C₂₋₄ substituted by hydroxy or amino.

or a pharmaceutically acceptable salt thereof.

49. (New) The compound of claim 48, wherein X is -NH-.

50. (New) The compound of claim 49, wherein R₁' is aryl, substituted aryl, aralkyl, substituted aralkyl, hetaryl, or substituted hetaryl,

51. (New) The compound of claim 3, wherein R₂ is lower alkyl optionally substituted

with one, two or three groups selected from hydroxy, alkoxy, halogen, amino, or acyl, or cycloalkyl optionally substituted with lower alkyl or alkoxy.

52. (New) The compound of claim 4, wherein R_3 is $-NR_4R_5$, in which R_4 and R_5 independently are hydrogen or lower alkyl optionally substituted with one, two or three groups selected from hydroxy, alkoxy, halogen, amino, or acyl.

53. (New) The compound of claim 5, wherein R_4 and R_5 independently are lower alkyl substituted with hydroxy or amino.

54. (New) The compound of claim 6, wherein R_4 and R_5 are both lower alkyl substituted with amino.

55. (New) The compound of claim 7, wherein R_4 and R_5 are both 2-aminoethyl.

56. (New) The compound of claim 8, wherein R_2 is lower alkyl.

57. (New) The compound of claim 9, wherein R_2 is isopropyl.

58. (New) The compound of claim 10, wherein R_1' is 4-methoxybenzyl, pyridin-3-ylmethyl, or cyclopropylmethyl.

59. (New) The compound of claim 8, wherein R_4 and R_5 are both lower alkyl substituted with hydroxy.

60. (New) The compound of claim 12, wherein R_4 and R_5 are both 2-hydroxyethyl.

61. (New) The compound of claim 13, wherein R_2 is isopropyl.

62. (New) The compound of claim 14, wherein R_1' is 4-phenylbenzyl, 4-

bromobenzyl, 4-bromoanilino, quinolin-3-yl, quinolin-5-yl, quinolin-6-yl, or quinolin-8-yl.

63. (New) The compound of claim 4, wherein R_1' is 4-methoxybenzyl or 3-phenylpropyl and R_3 is (R,S)-leucinol, L-histidinol, or (R)-2-amino-3-phenyl-1-propanol.

64. (New) The compound of claim 16, wherein R_2 is isopropyl.

65. (New) The compound of claim 2, wherein R_1' is lower alkyl, substituted lower alkyl, cycloalkyl, substituted cycloalkyl, heterocyclyl, or substituted heterocyclyl, R_2 is lower alkyl, and R_3 is $-NR_4R_5$, in which R_4 and R_5 independently are lower alkyl substituted with hydroxy or amino.

66. (New) The compound of claim 18, wherein R_1' is lower alkyl of 1-8 carbon atoms and R_2 is isopropyl.

67. (New) The compound of claim 18, wherein R_1' is cycloalkyl of 3-7 carbon atoms and R_2 is isopropyl.

68. (New) A method of treating a disease state in a mammal that is alleviable by treatment with a cell cycle kinase inhibitor, comprising administering to a mammal in need thereof a therapeutically effective dose of a compound of claim 1.

69. (New) The method of claim 21, wherein the cell cycle kinase inhibitor is CDK2.

70. (New) The method of claim 22, wherein the disease state is characterized by cell proliferation.

71. (New) The method of claim 23, wherein the disease state is rheumatoid arthritis, lupus, diabetes, multiple sclerosis, cancer, restenosis, graft-host disease, or gout.

72. (New) The method of claim 23, wherein the disease state is cancer.
73. (New) The method of claim 23, wherein the disease state is restenosis.
74. (New) The method of claim 21, wherein the cell cycle kinase inhibitor is $I\kappa B-\alpha$.
75. (New) The method of claim 27, wherein the disease state is inflammation

76. (New) A pharmaceutical composition comprising at least one pharmaceutically acceptable excipient and a therapeutically effective amount of a compound of claim 1.

REMARKS

Claims 48-76 are pending in this application. Favorable consideration and allowance of the application claims is courteously solicited.

Respectfully submitted,
McDONNELL BOEHNEN
HULBERT & BERGHOFF

Dated: August 14, 2001

By:


A. BLAIR HUGHES

Reg. No. 32,901

312-913-2123